REMARKS

1-Requirement for Restriction

The examiner required restriction to one of several groups of targets recited in the claims under 35 USC 1.121. The applicant has selected the receptor targets, as described above.

2- Amendment

THE CLAIMS

Claims 1-91 are pending in this application, and no claims have been amended. Consideration and allowance of these claims is requested.

THE SPECIFICATION

The applicant submitted with the Amendment of September 28, 2001, marked-up and clean copies of the amended specification pages. Further copies are enclosed herewith for the examiner's convenience. The amendments to the specification are fully supported by the specification, as filed and by the original claims. No objectionable new matter is believed to have been introduced by this amendment.
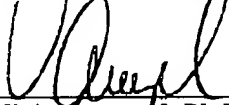
THE FEE

The Assistant Commissioner, however, is hereby authorized to charge to PTO Account No. 50-1728, the amount of $200.- for an extension fee of two months, which is herewith being requested. In view of the above amendments and remarks, this application is believed to be in condition for examination and allowance. Early notice to that effect is hereby solicited.

Respectfully submitted.
EPIGENESIS PHARMACEUTICALS, INC.

January 4, 2002

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Date

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification

Section beginning from page 296, line 56, to page 298, line 60, has been amended as follows (from next page):

GGATATAGGT TTCCAATTAA GTACATGGTC AAGTATTAAC AGCACAAGTG GTAGGTTAAC ATTAGAATAG
GAATTGGTGT TGGGGGGGGG GTTTGCAAGA ATATTTTATT TTAATTTTTT GGATGAAATT TTTATCTATT
ATATATTAAA CATTCTTGCT GCTGCGCTGC AAAGCCATAG CAGATTTGAG GCGCTGTTGA GGACTGAATT
ACTCTCCAAG TTGAGAGATG TCTTTGGGTT AAATTAAAAG CCCTACCTAA AACTGAGGTG GGGATGGGGA
5 GAGCCTTTGC CTCCACCATT CCCACCCACC CTCCCCTTAA ACCCTCTGCC TTTGAAAGTA GATCATGTTC
ACTGCAATGC TGGACACTAC AGGTATCTGT CCCTGGGCCA GCAGGGACCT CTGAAGCCTT CTTTGTGGCC
TTTTTTTTTT TTCATCCTGT GGTTTTTCTA ATGGACTTTC AGGAATTTTG TAATCTCATA ACTTTCCAAG
CTCCACCACT TCCTAAATCT TAAGAACTTT AATTGACAGT TTCAATTGAA GGTGCTGTTT GTAGACTTAA
CACCCAGTGA AAGCCCAGCC ATCATGACAA ATCCTTGAAT GTTCTCTTAA GAAAATGATG CTGGTCATCG
10 CAGCTTCAGC ATCTCCTGTT TTTTGATGCT TGGCTCCCTC TGCTGATCTC AGTTTCCTGG CTTTTCCTCC
CTCAGCCCCT TCTCACCCCT TTGCTGTCCT GTGTAGTGAT TTGGTGAGAA ATCGTTGCTG CACCCTTCCC
CCAGCACCAT TTATGAGTCT CAAGTTTTAT TATTGCAATA AAAGTGCTTT ATGCCCGAAT TC-3' (FRAG.NO:_)
(SEQ. ID NO:2497)
5' GCCGCCGCCA TGGGAGTGCA GGTGGAAACC ATCTCCCCAG GAGACGGGCG CACCTTCCCC AAGCGCGGCC
15 AGACCTGCGT GGTGCACTAC ACCGGGATGC TTGAAGATGG AAAGAAATTT GATTCCTCCC GGGACAGAAA
CAAGCCCTTT AAGTTTATGC TAGGCAAGCA GGAGGTGATC CGAGGCTGGG AAGAAGGGGT TGCCCAGATG
AGTGTGGGTC AGAGAGCCAA ACTGACTATA TCTCCAGATT ATGCCTATGG TGCCACTGGG CACCCAGCCA
TCATCCCACC ACATGCCACT CTCGTCTTCG ATGTGGAGCT TCTAAAACTG GAATGACAGG AATGGCCTCC
TCCCTTAGCT CCCTGTTCTT GGATCTGCCR TGGAGGGATC TGGTGCCTCC AGACATGTGC ACATGARTCC
20 ATATGGAGCT TTTCCTGATG TTCCACTCCA CTTTGTATAG ACATCTGCCC TGACTGAATG TGTTCTGTCA
CTCAGCTTTG CTTCCGACAC CTCTGTTTCC TCTTCCCCTT TCTCCTCGTA TGTGTGTTTA CCTAAACTAT
ATGCCATAAA CCTCAAGTTA TTCA-3' (FRAG. NO:_) (SEQ. ID NO:2498)

wherein B is adenosine, or, more preferably, replaces adenosine and is an "equivame\\lent" or a "universal"
base, and adenosine A_{2a} receptor agonist or only minimally antagonist, an adenosine A_{2b} receptor antagonist,
25 an adenosine A_3 receptor antagonist, or an adenosine A_1 receptor antagonist. Similarly, adenosine (A) may
always be replaced by an "alternative", "equivalent" and/or "universal" base having a small fraction,
preferably less than 0.3 of the activity of adenosine at the adenosine receptor(s), as described above.

In one preferred embodiment, the links between neighboring mononucleotides are phosphodiester
links. In another preferred, at least one mononucleotide phosphodiester residue of the anti-sense
30 oligonucleotide(s) is substituted by a methylphosphonate, phosphotriester, phosphorothioate,
phosphorodithioate, boranophosphate, formacetal, thioformacetal, thioether, carbonate, carbamate, sulfate,
sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, 2'-O-methyl,
methylene(methyimino), methylencoxy (methylimino), phosphoramidate residues, and combinations thereof.
The oligos having one or more phosphodiester residues substituted by one or more of the other residues are
35 generally longer lasting, given that these residues are more resistant to hydrolysis than the phosphodiester
residue. In some cases up to about 10%, about 30%, about 50%, about 75%, and even all phosphodiester
residues may be substituted (100%). Typically, the multiple target anti-sense oligonucleotide (oligo) of the
invention comprises at least about 7 mononucleotides, in some instances up to 60 and more mononucleotides,
preferably about 10 to about 36, and more preferably about 12 to about 21 mononucleotides. However, other
40 lengths are also suitable depending on the length of the target macromolecule. Examples of the MTA oligos of
the invention are provided in Table 3 below, which includes ninety-four sequences (SEQ ID NOS.: 2316
through 2410).

Table 3:	MTA Oligos, Location Targeted & Target			
MTA Oligo	**SEQ. ID No.**	**Location**	**Compound Targeted**	**Target**
HUMNFKBP65A AS				
CCC GGC CCC GCC TCG TGC C	3019	5'=1	EPI 2192	
CGT CCB TCC CGC CGG CCC	3020	5'=28 (AUG)	EPI 2193	
GCC CCG CTG CTT GGG CTG CTC TGC CGG G	3021	5'=65	EPI 2194	
TCT GTG CTC CTC TCG CCT GCC	3022	5'-137	EPI 2195	
TGC TGG GGT GGG TCT TGG TGG	3023	5'=159	EPI 2196	
CTG TCC CTG GTC CTG TG	3024	5'=196	EPI 2197	
GGT CCC GCT TCT TC	3025	5'=362	EPI 2198	
GGG GTT GTT GTT CGT CTG G	3026	5'=401	EPI 2199	
TGT CCT CTT TCT CC	3027[3026]	5'=656	EPI 2200	
GCC TCG GGC CTC CC	3028[3027]	5'=697	EPI 2201	
GGC TGG GGT CTG CGT	3029[3028]	5'=769	EPI 2202	

	GGC CGG GGG TCG GTG GGT CCG CTG	3030[3029]	5'-953	EPI 2203
	GGG CTG GGG TGC TGG CTT GGG G	3031[3030]	5'-1022	EPI 2204
	GGG GCT GGG GCC TGG GCC	3032[3031]	5'=1208	EPI 2205
	GCC TGG GTG GGC TTG GGG GC	3033[3032]	5'=1272	EPI 2206
5	GCT GGG TCT GTC CTG TTG CC	3034[3033]	5'=1362	EPI 2207
	CTT GTG TGG GGG GCC	3035[3034]	5'- 1451	EPI 2208
	GCT GGG TCG GGG GGC CTC TGC CCT GTC	3036[3035]	5'=1511	EPI 2209
	GCC CCG GGG CCC CC	3037[3036]	5'=1550	EPI 2210
	TGG CTC CCC CCT CC	3038[3037]	5'=1772	EPI 2211
10	GCT CCC CCC TTT CC	3039[3038]	5'=1863	EPI 2212
	CGG ACG AAG ACA GAG A	3040[3039]	5'=1979	EPI 2213
	GGC TTT GTC GGC TC	3041[3040]	6'=2011	EPI 2214
	GCC TGC TCT CCC CC	3042[3041]	5'=2312	EPI 2215
	CCC GGC CCC GCC BCG BBC C	3043[3042]	intron	EPI 2192-01A HSU50136C4Synth
15	CCC GGC CCC GCC BCG	3044[3043]	intron	EPI 2192-01B
	CCC GGC CCC GCC BCG BBC C	3045[3044]	5'untr	EPI 2192-02A HUMLIPOX5LO
	CCC GGC CCC GCC BCG	3046[3045]	5'untr	EPI 2192-02B
	CCC GBC CCC GCC TCB BG	3047[3046]	trans	EPI 2192-03A HSNFKBS Subunit
	CCC GBC CCC GCC TC	3048[3047]	trans	EPI 2192-03B
20	CCG GCC CCC CCT C	3049[3048]	5'untr	EPI 2192-04 TGFβR1
	CCC GBB CCC GCB TBG TGC C	3050[3049]	5'trans	EPI 2192-05A HSU581981l enhan
	CCC CCB TBG TGC C	3051[3050]	5'untr	EPI 2192-05B
	CCC GGB CCC BCC BBG TGC C	3052[3051]	3'trans	EPI 2192-06 HSVECAD
	CBG BBC CCG CCT CCT GCC	3053[3052]	intron	EPI 2192-07A NFKB2
25	C CCC CCT CCT CCC	3054[3053]	intron	EPI 2192-07B NFKD2
	CCG GCB CCG CCT CBT GCC	3055[3054]	5'trans	EPI 2192-08 Carboxypep
	CCG GCC CCG CCB CBT GCC	3056[3055]	3'trans	EPI 2192-09 HumADRA2Cα2Adrkid
	CCC GBC CCC GBC TCG	3057[3056]	5'untrs	EPI 2192-10 HUMFK506B
	CCC GGC CBC GBC TCG	3058[3057]	5'untrs	EPI 2192-11 HSNBARKS1βAdrKin
30	CCC GGC CCB GCC TBG	3059[3058]	5'UTR	EPI 2192-12 HSNFXN1(NFKB1)
	CCC GGC BCB GBC TCG TBC C	3060[3059]	3'UTR	EPI 2192-13 HSILF(transcrp. Factor ILF)
	CCC GGC CCC GCC BCG	3061[3060]		EPI-2192-14 NFKB/C4Syn/5-LO/ TGFBrec1 MTA
35	CCC GGC CCC GCC BCG	3062[3061]		EPI-2192-15NFKB/C4Syn/5-LOMTA
	TCC BTG CCG CGG GC	3063[3062]	3' trans	EPI-2193-01 METOncogene
	TCC BTG CCB CGG GCC	3064[3063]	3' trans	EPI-2193-02 HSFGR2(IG)
	TCC BTG CCB CGG GCC	3065[3064]	mid cod	EPI-2193-03 5-LO
	TCC BTG CCB CBG GCC	3066[3065]	mid cod	EPI-2193-04 HUMTK14
40	GTC CBT GBC CCG G	3067[3066]	3'trans	EPI-2193-05 HUMTNFR
	TC CBT GBC GCG GG	3068[3067]	AUG	Probl.HUMPTCH cardiacK+channel
	TCT GBG CTC CTC TBB CCT GGG	3069[3068]	intr	EPI-2195-01 humCSPAcytotox. Ser.Protease
45	CTG TGC BCC TBB CBC CTG GG	3070[3069]	intr	EPI-2195-02 HSINOSX08induc.NOS
	TGT GBT CCB CTB GBC TGG 0	3071[3070]		EPI-2195-03 HUMACHRM2musc.m2 acetylch.rec.
	TCT GTB CTC BBC TCB CCT G	3072[3071]		EPI-2195-04 s863718l Neurokinin3Recept
50	TGC TCC TCB CBB CTC GG inflam.factor	3073[3072] EPI-2195-05 HUMMIP1 Amacro		

MTA Oligo	SEQ. ID No.	Location	Compound Targeted	Target
CTC CTC TBG CCT GG	3074 [3073]		EPI-2195-06	HSNBARKS4
				β-Adr Rec Kinase
GTG CTC CBB TCB BCT GGG	3075 [3074]		EPI-2195-07	HSTNFR2S06TNF R2
CTG CBC CBB TCB CCT GGG	3076 [3075]		EPI-2195-08	humfkbp fk506
				binding prot.
TCT GTG CBC CTC TBG BCT	3077 [2076]	exon	EPI-2195-09	HSNBARKS1β-Adr.
				Recept.Kinase
CTC TBB TCC TBB CBC CTG G	3078 [3077]	intron	EPI-2195-10	HUMIL8
TCT GCT BBT CBC BCB TCG G	3079 [3078]		EPI-2195-11	HSU50157 PDE4
GTC CBC CBC TCB CCT G	3080 [3079]	intron/exon	EPI-2195-12	IL-2 R
CTG TGC BCC TCT C	3081 [3080]	3'UTR	EPI-2203-05	IL-6 R HSIL6R
CBG TGC BCC BCT CBC CTG	3082 [3081]	intr/ex	EPI-2203-06A	HSIL2rG6
G TGC BCC BCT CBC CTG	3083 [3082]	intr/ex	EPI-2203-06B	HSIL2rG6
CBC CTC TCB CCT GGG	3084 [3083]	coding	EPI-2203-07A	HUMIL71
C CTC TCB CCT GGG	3085 [3084]	coding	EPI-2203-07B	IL-7 HUMIL71
GCT CCB CTC GCC T	3086 [3085]	coding	EPI-2203-08	IL-6 R HSI6REC
TGC TCC TCB CGC C	3087 [3086]	intron PDGF A	EPI-2303-09	Chain HUMPDGFAB
GTT GTT GBT CTG G	3088 [3087]	3'utr	EPI-2199-01	GATA-4Transcrip
				Factor for IL-5
GGT TGB BBT TGG TCT TGC	3089 [3088]	Coding	EPI-2199-02	TNFα HUMTNFA
GGT TGT TGB TGB TCT G	3090 [3089]	far 5'UTR	EPI-2199-03	HSSUBP1G(Sub Pr)
GGG TTB BBG TTG BTC TGG	3091 [3090]	Coding	EPI-2199-04	NeutrophilAdh.
				R HUMNARIA
GGG TTB BBG TTG BTC TGG	3092 [3091]	HSHM2	EPI-2199-05	m2 Muscarinic R
TTG TTG TBG BTC TGG	3093 [3092]	HUML1CAM	EPI-2199-06	L1 LeukAadhProt
GGG TBG BBG BGT CCG CTG	3094 [3093]	coding	EPI-2203-01	HUMGATA2A
GGG TCB GBG GBT CBG CTG	3095 [3094]	S71424S2	EPI-2203-02	IGE cps
GGG TBG GTG GGT C	3096 [3095]	coding	EPI-2203-03	HSGCSFR2
GGG TCG GBG GGT CBG C	3097 [3096]	HUMITGF	EPI-2203-04	TGFβ3
GGG TGG CCT T	3098 [3097]	HUMNK6SPRO	EPI-2206-01	NFKB/NK &
				TCell
				Activating Prot
GGG TGG GCT TGG G	3099 [3098]	HUMPEREEB	EPI 2206-02	NFKB/Prostagl.
				EP3 Rec
CCTGGGTGGGBBTGGC	3100 [3099]		EPI 2206-03	HSNF2B/GCSF
				NFKB/GranuLocCSF/
				Transcr.FactorNF2B
CCTCGBTCGGCBTGGC	3101 [3100]		EPI-2206-04	HUMLAP/NFKB
				Leuk.Adhes.Prot
GCCTGBGTGBBCTTCGC	3102 [3101]		EPI2206-05	NFKB/Endothel
				N2 S63833
CCCAVGVCCVCCCAGGC	3103 [3102]		EPI 2206-06	NFKBAS13/B Lymph
				SerThrProt.Kinase
AGCCCACCCAGGC	3104 [3103]		EPI2206-07	NFKBAS13/GCSF1
				HSGCSFR1Rec
BCCTGGGTCGGCTB	3105 [3104]		EPI2206-08	NFKBAS13/GCSF1/
				NK7TCELLACT.Prot
GGTGGGCTTGGG	3106 [3105]		EPI 2206-09	NFKBAS13/
				HSTGFB1 TGFB
CCBBGGTGGGCTTGGG	3107 [3106]		EPI 2206-10	NFKBAS13/
				HSTGFB1 TGFB1
CTGGGTGGGBBTGGG	3108 [3107]		EPI 2206-11	NFKBAS13/
				HSGCSFR1 GCSFR1
CCBGGGTGGGCTTGG	3109 [3108]		EPI 2206-12	NFKBAS13/HUMCD30A
				LymphActAntigCoding
GGGTGGGCTTGG	3110 [3109]		EPI-2206-12B	NFKBAS13/HUMCD30A
CCTGBGTGBGCBTGGG	3111 [3110]		EPI 2206-13	NFKBAS13/HUMCAM1V
				Vasc.Endoth.Cell
				Adh.Molec

B: Universal Base

The MTA oligos of Table 3 are suitable for use with two or more of the targets listed in Table 4 below.

CLEAN VERSION

In the specification

Please enter the following pages 296 through 298 for the substitution of the previous original pages (starting from next page):